REMARKS

Claims 3, 4, and 56 are currently pending in the present application, and claims 3 and 56 have been amended herein. Claims 1, 2, 5-55, and 57-63 were withdrawn as being directed to a non-elected invention.

Objection to Priority Information

Applicants have amended the "Cross Reference to Related Applications" section to reflect that parent U.S. Application No. 09/590,837, to which the present application claims priority, is abandoned.

Applicants request that this objection be withdrawn in view of the amendment.

Objection to the Drawings

Applicants submit herewith a copy of Figure 5 showing amygdala RNA from various rats as described in the Figure legend. Applicants respectfully request reconsideration and withdrawal of this objection.

Rejection of claims 3 and 4 in view of 35 U.S.C. §101

Claims 3 and 4 have been rejected by the Examiner as being non-statutory subject matter because the claimed WLI rat is apparently indistinguishable from a product of nature. Applicants respectfully traverse this rejection.

Applicants have amended claim 3 to recite that the claimed WLI rat is obtained from at least the F2 generation of a mating between two commercially available WKY rats selected on the basis of their forced swim score. Page 12, beginning at line 28, indicates that the WLI substrain of rats does not exist in nature. The individual rats of the WLI substrain, particularly those rats in the F2 generation and higher, exhibit very similar behavioral phenotypes, which are distinctly different from the parental strain.

The careful selective mating by the inventors of two parental and F1 generation WKY rats, each having a FST score of 8 or lower, makes the production of F2 and higher generations non-random and reproducible. Additional data presented in the Declaration of Dr. Eva Redei, a co-inventor of the present application, demonstrates the

reproducibility of obtaining WLI rats having FST scores of less than 8 or 6 in F2 and higher generations.

Therefore, the WLI rat claimed in the instant invention is distinguishable from a product of nature because the selective mating of rats of the parental and F1 generation is not random. For this reason, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejection of claims 3, 4, and 56 in view of 35 U.S.C. §112, first paragraph, enablement

The Examiner has rejected claims 3, 4, and 56 as lacking enablement because, in the Examiner's view, the specification fails to teach the frequency of finding a WKY rat with the low FST score in a WKY rat population, and fails to teach the predictability and persistency of obtaining the recited trait in progenies of the F2 generation and above. In the Examiner's view, this places a burden of undue experimentation on a practitioner of the present invention to determine the reproducibility and predictability of these parental matings. Applicants respectfully traverse this rejection.

Applicants provide herein a Declaration of inventor Dr. Eva Redei. Dr. Redei conducted several post-filing experiments that indicate the reproducibility of obtaining a WLI rat having an FST score of less than about 8 or less than about 6 in the F2 generation or higher. The Declaration recites that the difference in FST score between the F2 and higher generations and the parental generation is highly significant. In addition, Figure 1 of the Declaration indicates that WLI rats from at least the F2 generation out to the F7 generation retain the trait of having an FST score of less than about 8. Therefore, Applicants have demonstrated that these results are predictable and reproducible through at least the F7 generation, and likely are reproducible throughout the breeding process.

WLI rats are genetically different and selectively bred from the WKY parental strain, the functional characteristic for selection being the FST score. As pointed out in the specification at page 38 in Example 1, WKY parents having specific FST scores are mated to produce an F1 generation. The F1 generation is then selectively bred, based on the FST scores, to produce the WLI substrain of rat claimed in the present

invention. The results of the experiments in Example 1 demonstrate that selective breeding of F1 rats having low FST scores produced rats having even lower FST scores than the parental strain. In essence, a substrain of rats having a less depressive phenotype is produced. As indicated beginning on page 12, line 28, the individual rats of the WLI substrain exhibit very similar behavioral phenotypes, which are distinctly different from the parental strain. These experiments are reproducible as demonstrated by the results provided in the Declaration.

For these reasons, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejection of claims 3 and 4 in view of 35 U.S.C. §102(b)

The Examiner has rejected claims 3, 4, and 56 as being anticipated by *Paré, et al., Physiol & Behav, 62(3):643-648 (1997).* In the Examiner's view, *Paré* et al. disclose WKY rats that are hyper-responsive to stress and prone to stress ulcer. In addition, the Examiner points out that WKY rats have been inbred for quite some time, and many generations of rats have been produced. Thus, in the Examiner's view, the progeny of those inbreedings would inherently exhibit less depressive behavior and have an FST of lower than about 8. Applicants respectfully disagree with the Examiner's analysis.

Paré et al. teach that WKY rats from different suppliers display different responses to stress. *Paré* merely purchased rats from four different suppliers and demonstrated that WKY rats from different suppliers react differently to stress. There is no selective mating of WKY rats taught in *Paré*. Applicants contend that the claimed animals are not the product of inbreeding. Rather, these claimed animals are the product of selective breeding. As dicussed above, the WLI rats are genetically different and selectively bred from the WKY parental strain, the functional characteristic for selection being the FST score. As pointed out in the specification at page 38 in Example 1, WKY parents having specific FST scores are mated to produce an F1 generation. The F1 generation is then selectively bred, based on the FST scores, to produce the WLI substrain of rat claimed in the present invention. The results of the experiments in Example 1 demonstrate that selective breeding of F1 rats having low FST scores

produced rats having even lower FST scores than the parental strain. In essence, a substrain of rats having a less depressive phenotype is produced. As indicated beginning on page 12, line 28, the individual rats of the WLI substrain exhibit very similar behavioral phenotypes, which are distinctly different from the parental strain. These experiments are reproducible as demonstrated by the results provided in the Declaration of Dr. Redei, included herewith.

Paré does not teach selective breeding based on FST scores. Therefore, *Paré* does not anticipate the present invention. Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of claims 3, 4, and 56 in view of 35 U.S.C. §102(a)

The Examiner has rejected claims 3, 4, and 56 as being anticipated by *Begum, et al.* In the Examiner's view, *Begum* teaches WKY rats as discussed above for *Paré*, and also teaches obtaining cells from the WKY rat. Applicants respectfully disagree with the Examiner's contention.

As described elsewhere herein, the claims of the present invention have been amended to recite that the claimed WLI rat is at least the F2 product of a selective mating between two WKY rats having a specific FST score. The WLI substrain of rats created by this selective mating displays a specific phenotype very different from the parental strain of WKY rat. *Begum* does not teach this selective breeding, nor does Begum use the FST test in any of his experiments. Therefore, Begum does not teach the present invention.

In addition, because the F2 or higher generation WLI rat has a significantly different phenotype than the parental WKY rats and the phenotype is genetically transmissible, it is implied that the genotype of this substrain of rats is also different. Hence, the cells of such WLI rats are different than those of the parental WKY rats. Therefore, *Begum* does not anticipate the claims.

Applicants request that the Examiner reconsider and withdraw the rejection.

Summary

Applicants respectfully submit that each rejection of the Examiner to the claims of the present application has been overcome or is now inapplicable, and that claims 3, 4, and 56 are in condition for allowance. Reconsideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,

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